IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Havenga et al.

Serial No.: To be assigned

Filed: January 7, 2002

For: INFECTION WITH CHIMAERIC ADENOVIRUSES OF CELLS NEGATIVE FOR THE ADENOVIRUS SEROTYPE 5 COXSACKI ADENOVIRUS RECEPTOR (CAR)

Examiner: To be assigned

Group Art Unit: To be assigned

Attorney Docket No.: 5226US

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PRELIMINARY AMENDMENT

Commissioner for Patents Washington, D.C. 20231

Sir:

Please amend the above identified patent application as follows:

IN THE CLAIMS:

Please amend the claims (without prejudice or disclaimer) as follows. Please note that claim amendments are presented here in clean form for clarity, a marked up version of the claim amendments is attached.

Please cancel claims 2 and 17 without prejudice or disclaimer.

- 5. (Amended) The chimeric gene delivery vehicle of claim 3, further comprising: an element from adenovirus 35 responsible for at least partially avoiding an immune response against adenovirus 35 in man.
- 6. (Amended) The chimeric gene delivery vehicle of claim 5, comprising an adenoviral 16 element or a functional analogue thereof, said adenoviral 16 element conferring adenovirus 16 with an enhanced capability to infect smooth muscle cells and/or synoviocytes.
- 7. (Amended) The chimeric gene delivery vehicle of claim 3, further comprising adenoviral nucleic acid.
- 8. (Amended) The chimeric gene delivery vehicle of claim 3, further comprising adenoviral nucleic acid derived from at least two different adenoviral types.
- 9. (Amended) The chimeric gene delivery vehicle of claim 8, wherein said adenoviral nucleic acid comprises at least one sequence encoding a capsid protein comprising at least a tissue tropism determining fragment of adenovirus subgroup D and/or adenovirus subgroup F capsid protein.
- 10. (Amended) The chimeric gene delivery vehicle of claim 9, wherein said adenoviral nucleic acid is modified to reduce or disable the ability of said adenoviral nucleic acid to replicate in a target cell.
- 11. (Amended) The chimeric gene delivery vehicle of claim 7, wherein said adenoviral nucleic acid has been modified to reduce or disable the capacity of a host immune system to mount an immune response against adenoviral proteins encoded by said adenoviral nucleic acid.
- 12. (Amended) The chimeric gene delivery vehicle of claim 7, comprising a minimal adenovirus vector or an integrating adenovirus.

- 13. (Amended) The chimeric gene delivery vehicle of claim 7 further comprising at least one non-adenoviral nucleic acid.
- 14. (Amended) The chimeric gene delivery vehicle of claim 8 wherein said adenoviral nucleic acid is produced by a process comprising:

welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said partially overlapping sequences allowing essentially only a single homologous recombination event thus generating a physically linked nucleic acid comprising:

a nucleic acid of interest, at least two functional adenoviral inverted terminal repeats (ITRs), and a functional encapsulation signal, or functional parts, derivatives or analogues of said ITRs and/or encapsulation signal.

15. (Amended) A cell for producing the chimeric gene delivery vehicle of claim 3, said cell comprising:

first means for assemblying said gene delivery vehicle wherein said first means includes further means for producing of an adenovirus capsid protein, said capsid protein comprising at least a receptor and/or binding site binding fragment of adenovirus subgroup D and/or adenovirus subgroup F capsid protein.

22. (Amended) An isolated and/or recombinant nucleic acid encoding a capsid protein of claim 20.

Remarks

The Office is respectfully requested to enter the above amendments prior to the calculation of the filing fee in this application. The amendments and claim cancellations are made without prejudice or disclaimer. The amendments merely remove multiple dependencies. Should the Office determine that additional issues remain which might be resolved by a telephone conference, it is respectfully invited to contact applicants' undersigned attorney.

Respectfully Submitted,

Allen C. Turner

Registration Number 33,041

Attorney for Applicants

TRASKBRITT, PC

P.O. Box 2550

Salt Lake City, Utah 84110

Telephone: (801) 532-1922

Date: January 7, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please amend the claims as follows:

- 5. (Amended) The chimeric gene delivery vehicle of claim 3 [or claim 4], further comprising: an element from adenovirus 35 responsible for at least partially avoiding an immune response against adenovirus 35 in man.
- 6. (Amended) The chimeric gene delivery vehicle of [any one of claims 3-5] claim 5, comprising an adenoviral 16 element or a functional analogue thereof, said adenoviral 16 element conferring adenovirus 16 with an enhanced capability to infect smooth muscle cells and/or synoviocytes.
- 7. (Amended) The chimeric gene delivery vehicle of [any one of claims 3-6] claim 3, further comprising adenoviral nucleic acid.
- 8. (Amended) The chimeric gene delivery vehicle of [any one of claims 3-7]claim 3, further comprising adenoviral nucleic acid derived from at least two different adenoviral types.
- 9. (Amended) The chimeric gene delivery vehicle of [claim 7 or] claim 8, wherein said adenoviral nucleic acid comprises at least one sequence encoding a capsid protein comprising at least a tissue tropism determining fragment of adenovirus subgroup D and/or adenovirus subgroup F capsid protein.
- 10. (Amended) The chimeric gene delivery vehicle of [claim 7, claim 8, or] claim 9, wherein said adenoviral nucleic acid is modified to reduce or disable the ability of said adenoviral nucleic acid to replicate in a target cell.
- 11. (Amended) The chimeric gene delivery vehicle of claim 7, [claim 8, claim 9, or claim10,] wherein said adenoviral nucleic acid has been modified to reduce or disable the capacity of a host

immune system to mount an immune response against adenoviral proteins encoded by said adenoviral nucleic acid.

- 12. (Amended) The chimeric gene delivery vehicle of claim 7, [claim 8, claim 9, claim 10, or claim 11,] comprising a minimal adenovirus vector or an integrating adenovirus.
- 13. (Amended) The chimeric gene delivery vehicle of [any one of the claims 1-12,]claim 7 further comprising at least one non-adenoviral nucleic acid.
- 14. (Amended) The chimeric gene delivery vehicle of [any one of claims 7-13,]claim 8 wherein said adenoviral nucleic acid is produced by a process comprising:

welding together, through homologous recombination, two nucleic acid molecules comprising partially overlapping sequences wherein said partially overlapping sequences allowing essentially only a single homologous recombination event thus generating a physically linked nucleic acid comprising:

a nucleic acid of interest, at least two functional adenoviral inverted terminal repeats (ITRs), and a functional encapsulation signal, or functional parts, derivatives or analogues of said ITRs and/or encapsulation signal.

15. (Amended) A cell for producing the chimeric gene delivery vehicle of [any one of the claims 3-14] claim 3, said cell comprising:

first means for assemblying said gene delivery vehicle wherein said first means includes further means for producing of an adenovirus capsid protein, said capsid protein comprising at least a receptor and/or binding site binding fragment of adenovirus subgroup D and/or adenovirus subgroup F capsid protein.

22. (Amended) An isolated and/or recombinant nucleic acid encoding a capsid protein of claim 20 [or claim 21].